REMARKS

Interview

Applicants thank Examiner Kifle for his time and attention in the personal interview held on December 3, 2003. In the Interview, Applicants' representative proposed claim amendents to overcome the indefinite rejections. Arguments against the enablement rejection were presented. Applicants' representative proposed providing Declaration evidence to support the arguments. The Examiner's comments and suggested amendments have been incorporated herein.

Status of the Claims

Claims 1, 13, 24-26 and 34 are pending in this application. Claims 2-12, 14-23 and 27-33 have been canceled. Claim 34 has been added. The claims have been amended to recite that A is oxygen, R^1 is a phenyl having an N, N-di-lower alkylaminoalkoxy group or morpholinyl-lower alkoxy group, pyridyl group or a pyridyl group having a halogen atom, hydroxy group, a lower alkyl group or a lower alkoxy group; R^2 is phenyl, a phenyl having a halogen atom, pyridyl group or pyridyl having nitril group; and R^4 and R^5 are hydrogen. The method claims have also been amended to delete particular diseases included in the Markush group of treatable diseases. Support for new claim 34 is found in examples 1, 33, 34,

42, 54, 61, 66 and 68. No new matter has been added by the above claim amendments.

Rejections under 35 USC 112, second paragraph

The Examiner rejects claims 1-16, 22-26, 32 and 33 as indefinite for the definition of the heteroaryl group because the heteroatom(s) is/are not defined. Applicants amend the claims so that heteroatoms no longer appear in the claims. As such, Applicants request that this rejection be withdrawn.

Rejection under 35 USC 112, first paragraph

The Examiner maintains the rejection of claims 24-26 as not enabled for treating and ameliorating "nerve degeneration diseases" generally. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants amend claims 24-26 to delete certain nerve degeneration diseases that the Examiner questions, such as ALS, Alzheimer's disease, Parkinson's etc. Applicants also submit that the subject matter of claims 24-26 is supported by pharmacological tests 3 and 4 in the specification at pages 113-115. Test 3 supports the treatment of epilepsy and test 4 supports treatment of acute nerve degeneration after cerebral ischemia.

Applicants also submit the following test data submitted in the attached Declaration under 37 CFR 1.132 by Mr. Hanada to demonstrate that Applicants' invention was enabled at the time the present application was filed. Please see paragraphs 2-3 of the Declaration.

Applicants conducted a Formalin test to support the treatment of pain. Applicants also conducted an EAE test to support the treatment of multiple sclerosis and other related diseases. In the Formalin test, the analgesic effect of the compound of claim 1, particularly compound # 54 was tested. In the test, mice were injected with formalin. The mice demonstrated pain related licking and biting behavior. These responses were measured over time. Compound #54 was found to reduce the pain related licking and biting in the mice. The results of the test are graphed in Table 1 in the Declaration.

Likewise, Applicants conducted an EAE test on Lewis rats immunized with an inoculum containing MBP emulsified in Freund's complete adjuvant containing *M. tuberculosis*. The rats were then given Compound #1 over 9 days. The rats were observed for symptoms of multiple sclerosis, such as half paralyzed tail, unsteady gait, paralysis of hind limbs, etc. Once the rats were administered Compound #1, the rats' symptoms subsided and

returned to normal. The results are reported in Table 2 in the Declaration.

Applicants submit that the invention of claims 24-26 is enabled by the specification. As such, Applicants respectfully request that the Examiner withdraw the enablement rejection.

Rejection under 35 USC 103(a)

The Examiner maintains the rejection of claim 1 as obvious over Dekeyser et al. USP 4,670,555 (Dekeyser '555). The Examiner states in the Office Action that the samples tested in the Declaration are not the closest prior art because the compounds of samples 074 and 125 have a pyridyl group whereas the comparative (prior art) samples tested do not have this pyridyl group.

Applicants traverse the rejection and submit the following arguments in support of the patentability of the claims over Dekeyser '555.

Applicants amend the claims to recite that, in Formula I, A is oxygen, R^1 is a phenyl having an N, N-di-lower alkylaminoalkoxy group or morpholinyl-lower alkoxy group, pyridyl group or a pyridyl group having a halogen atom, hydroxy group, a lower alkyl group or a lower alkoxy group; R^2 is a phenyl, a phenyl having a halogen atom, a pyridyl group or a pyridyl having nitril group; and R^3 and R^4 are both hydrogen. Applicants submit that the presently claimed

invention is patentable over Dekeyser '555 as Dekeyser '555 fails to disclose a compound similar to Formula I and fails to suggest making the necessary modifications to arrive at a compound of Formula I as in the present invention.

Applicants also submit herewith a Declaration by Mr. Hanada attesting to differences between the compound of the present invention and the compound of Dekeyser '555. Please see paragraph 4 and Table 3 of Mr. Hanada's Declaration which compares similar compounds from Dekeyser '555 and compounds of claim 34. Each compound from Dekeyser '555 was tested *in vitro* and *in vivo*. The IC50 of each compound was measured in the *in vitro* assay and the number of spasmed mice was measured in the *in vivo* assay. Please note that in the *in vivo* assay for the present invention, the results are an unexpected significant improvement over the compounds of Dekeyser '555. In Dekeyser '555, at least half or all of the mice showed seizures as compared to the present invention where, at most, only one mouse had seizures. Likewise, the IC50 values are unexpected improvements over the compounds of Dekeyser '555.

Applicants submit that this data supports that the present invention is non-obvious over Dekeyser '555. As such, Applicants respectfully request that this rejection be withdrawn.

Conclusion

As Applicants have addressed and overcome all rejections in the Office Action, Applicants respectfully request that the rejections be withdrawn and that the claims be allowed.

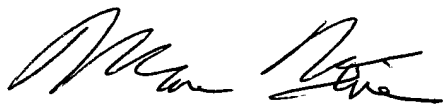
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kecia Reynolds (Reg. No. 47,021) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $420.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 
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Attachment(s): Declaration under 37 C.F.R. §1.132

(Rev. 09/30/03)